2/9/49 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences

01641955 INSIDE CONFERENCE ITEM ID: CN016741571
Leukemia cells derived from relapsed and/or refractory patients that express multidrug resistant protein P-gp 170 are sensitive to lysis by natural killer cell line **NK-92**
Yan, Y.; Koo, K.; Collins, N. H.; O'Reilly, R. J.
CONFERENCE: American Society of Hematology-Annual meeting; 38th
BLOOD -NEW YORK-, 1996; VOL 88; NUMBER 10//S1A P: 1446
Saunders, 1996
ISSN: 0006-4971
LANGUAGE: English DOCUMENT TYPE: Conference Prepinted abstracts and programme
CONFERENCE SPONSOR: American Society of Hematology
CONFERENCE LOCATION: Orlando, FL
CONFERENCE DATE: Dec 1996 (199612) (199612)

BRITISH LIBRARY ITEM LOCATION: 2112.000000
DESCRIPTORS: hematology; ASH

2/9/55 (Item 3 from file: 159)
DIALOG(R)File 159:Cancerlit

01144179 96606702
Human natural killer (NK) cells induce the expression of E-selectin and interleukin 8 MRNA in porcine endothelial cells (Meeting abstract).
Goodman DJ; von Albertini M; Bach FH
Sandoz Center for Immunobiology, Harvard Medical School, Boston, MA 02215
FASEB J; 9(4):A792 1995 ISSN 0892-6638
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
Journal Announcement: 199605
Subfile: ICDB/96606702
NK cells display a wide spectrum of cytotoxicity towards virally-infected cells, malignant cells and some xenogeneic targets. Activation and damage of endothelial cells (EC's) in the rejecting xenograft appears to underlie the rejection process and NK cells have been demonstrated in rejecting discordant xenografts. To determine if NK cells may be pathogenetically involved in rejection, we have assessed, in vitro, whether human NK cells activate porcine EC's, as measured by induction of the adhesion molecule E-selectin and the chemotactic cytokine, Interleukin 8 (IL-8). We studied co-cultures containing human NK cells, used immediately after isolation from blood, and confluent porcine EC monolayers. After 4 hr of co-culture, RNA was extracted followed by RT/PCR for E-selectin and IL-8 MRNA expression. The expression of E-selectin and IL-8 secretion was confirmed by ELISA. NK cells added to pEC's resulted in significant cellular cytotoxicity at effector to target (E:T) ratios greater than 5:1. At lower NK porcine EC (E:T) ratios, Ecs were activated with the induction of both E selectin and IL-8 MRNA expression. The induction of E-selectin and IL-8 MRNA was seen with three separate sources of NK cells: purified CD56+ve cells, the B22 cell clone and the **NK92** cell line. The addition of human soluble TNF-alpha receptor failed to inhibit the induction of E-selectin. Thus, human NK cells, at E:T ratios below those associated with cytotoxicity activate porcine EC resulting in the expression of E-selectin and IL-8 secretion implicating NK cells in EC activation and cell mediated xenograft rejection.
CAS Registry No.: 0 (E-Selectin); 0 (Interleukin-8); 0 (RNA, Messenger)

2/9/36 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10732016 BIOSIS NO.: 199799353161
In-vitro and in-vivo anti-leukemic activity of a natural killer (NK) cell clone against both primary human leukemias and leukemic cell lines.
AUTHOR: Yan Y; McGuirk J; Steinherz P; O'Reilly R J
AUTHOR ADDRESS: Bone Marrow Transplantation Service, Memorial Sloan-Kettering Cancer Center, New York, NY**USA
JOURNAL: Blood 88 (10 SUPPL. 1 PART 1-2):p245A 1996
CONFERENCE/MEETING: Thirty-eighth Annual Meeting of the American Society of Hematology Orlando, Florida, USA December 6-10, 1996
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics (Transport and Circulation); Cell Biology; Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Poster; ANTI-LEUKEMIC ACTIVITY; BLOOD AND LYMPHATIC DISEASE; CLINICAL IMMUNOLOGY; HUMAN NATURAL KILLER CELL; LEUKEMIA; NEOPLASTIC DISEASE; **NK-92** CELL LINE; ONCOLOGY; PATIENT
CONCEPT CODES:
02508 Cytology and Cytochemistry-Human
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
15006 Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and Reticuloendothelial Pathologies
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
24003 Neoplasms and Neoplastic Agents-Immunology
24010 Neoplasms and Neoplastic Agents-Blood and Reticuloendothelial Neoplasms
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
86215 Hominidae

2/9/39 (Item 39 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10214884 BIOSIS NO.: 199698669802
Activation of protein tyrosine phosphorylation in the human NK cell line **NK-92** via ICAM-3 and CD44.
AUTHOR: Maki Guitta; Dougherty Graeme; Takei Fumio; Klingeman Hans
AUTHOR ADDRESS: Terry Fox Lab., BC Cancer Agency, Vancouver, BC**Canada
JOURNAL: Natural Immunity 14 (2):p83 1995
CONFERENCE/MEETING: Third International Workshop of the Society for Natural Immunity on NK Cells and Natural Immunity Oxnard, California, USA December 2-6, 1995
ISSN: 1018-8916

RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 60-18-4: TYROSINE
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Membranes (Cell Biology); Metabolism
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Hominidae (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
CHEMICALS & BIOCHEMICALS: TYROSINE
MISCELLANEOUS TERMS: ADHESION MOLECULES; HUMAN NATURAL KILLER CELL LINE **NK-92**; INTERCELLULAR ADHESION MOLECULE-3; MEETING ABSTRACT; NATURAL IMMUNITY; SIGNAL-TRANSDUCING MOLECULES
CONCEPT CODES:
02508 Cytology and Cytochemistry-Human
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
10506 Biophysics-Molecular Properties and Macromolecules
10508 Biophysics-Membrane Phenomena
13002 Metabolism-General Metabolism; Metabolic Pathways
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10054 Biochemical Methods-Proteins, Peptides and Amino Acids
10058 Biochemical Methods-Carbohydrates
32500 Tissue Culture, Apparatus, Methods and Media
32600 In Vitro Studies, Cellular and Subcellular
BIOSYSTEMATIC CODES:
86215 Hominidae

2/9/40 (Item 40 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09639742 BIOSIS NO.: 199598094660
Proliferation of hematopoietic cell lines induced by a soluble factor derived from human squamous cell carcinomas of the head and neck.
AUTHOR: Yasumura Satoshi; Amoscato Andrew; Hirabayashi Hideki; Lin Wen Chang; Whiteside Theresa L
AUTHOR ADDRESS: Pittsb. Cancer Inst., W1041 Biomedical Science Tower, 211 Lothrop St., Pittsburgh, PA 15213-2582**USA
JOURNAL: Cancer Immunology Immunotherapy 39 (6):p407-415 1994
ISSN: 0340-7004
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The supernatant of a cell line of squamous cell carcinoma of the head and neck (SCCHN), PCI-50, was previously shown to induce activation, promote proliferation and increase antitumor cytotoxicity of freshly purified human natural killer (NK) cells and CD4+ T lymphocytes (Arch Otolaryngol Head Neck Surg (1994) in press). This supernatant was found also to promote the growth of a variety of hematopoietic cell lines, including Jurkat, THP-1, K562, **NK-92** or Epstein-Barr-virus-transformed B cell lines. The Jurkat cell line was selected as a reporter cell in an 18-h proliferation assay established to measure the growth-promoting activity of PCI-50 supernatant. The presence of soluble tumor-derived factors able to induce proliferation of Jurkat

cells was demonstrated in the supernatant produced by several other SCHHN cell lines but not in that produced by a gastric cancer cell line (HR) or renal cell carcinoma line (5117G8). The growth-promoting PCI-50 supernatant was shown to contain 28 +- 0.5 pg/ml interleukin-6 (IL-6) in vitro but was negative for interferon, gamma, IL-1, IL-2, IL-4, tumor necrosis factor alpha, granulocyte/macrophage-colony-stimulating factor and IL-12. The addition of any of these recombinant cytokines to Jurkat cell cultures did not significantly promote growth, while PCI-50 supernatant was consistently growth-stimulatory. This supernatant neither enhanced intracellular Ca-2+ concentration in Jurkat cells nor induced up-regulation of activation antigens on the cell surface, although it supported growth of Jurkat cells in the absence of IL-2. The growth-promoting activity in the PCI-50 supernatant was acid-labile at pH 2 for 4, heat-resistant at 96 degree C for 1 h and sensitive to treatments with trypsin and pepsin. Preincubation of the PCI-50 producer cells with tunicamycin or cyclohexamide reduced the level of growth-promoting activity in the supernatant. A partial purification of this activity was achieved using Amicon filtration, chromatography on concanavalin-A-Sepharose and then a hydroxyapatite column and high-pressure liquid chromatography gel filtration. The partially purified glycoprotein had a molecular mass of 50-70 kDa, as determined by gel filtration.

DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Hematology (Human Medicine, Medical Sciences); Metabolism; Morphology; Oncology (Human Medicine, Medical Sciences)
BIOSYSTEMATIC NAMES: Herpesviridae--Viruses; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Epstein-Barr virus (Herpesviridae); JURKAT (Hominidae)--cell line; K-562 (Hominidae)--cell line; THP-1 (Hominidae)--cell line
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; microorganisms; primates; vertebrates; viruses
MISCELLANEOUS TERMS: INTERLEUKIN 6; **NK-92** LEUKEMIA CELLS
CONCEPT CODES:
02508 Cytology and Cytochemistry-Human
11304 Chordate Body Regions-Head (1970-)
11308 Chordate Body Regions-Neck (1970-)
13004 Metabolism-Carbohydrates
13012 Metabolism-Proteins, Peptides and Amino Acids
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
15006 Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and Reticuloendothelial Pathologies
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
17002 Endocrine System-General
24005 Neoplasms and Neoplastic Agents-Neoplastic Cell Lines
24006 Neoplasms and Neoplastic Agents-Biochemistry
24010 Neoplasms and Neoplastic Agents-Blood and Reticuloendothelial Neoplasms
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10068 Biochemical Studies-Carbohydrates
14006 Digestive System-Pathology
15506 Urinary System and External Secretions-Pathology
24007 Neoplasms and Neoplastic Agents-Carcinogens and Carcinogenesis
25508 Developmental Biology-Embryology-Morphogenesis, General
32500 Tissue Culture, Apparatus, Methods and Media
33506 Virology-Animal Host Viruses
36006 Medical and Clinical Microbiology-Virology
BIOSYSTEMATIC CODES:
02612 Herpesviridae (1993-)
86215 Hominidae

2/9/48 (Item 1 from file: 35)

01631277 ORDER NO: AADNQ-25105
MECHANISM OF LEUKEMIC CELL KILLING BY IL-2 ACTIVATED NATURAL KILLER CELLS, ROLE OF CELL ADHESION MOLECULES (INTERLEUKIN-2)

Author: MAKI, GUITTA
Degree: PH.D.
Year: 1997
Corporate Source/Institution: THE UNIVERSITY OF BRITISH COLUMBIA (CANADA) (2500)
Advisers: HANS KLINGEMANN; FUMIO TAKEI
Source: VOLUME 59/02-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 595. 179 PAGES
Descriptors: HEALTH SCIENCES, IMMUNOLOGY
Descriptor Codes: 0982
ISBN: 0-612-25105-5

Natural killer (NK) cells and lymphokine activated NK (LAK) cells, contribute to the elimination and growth control of malignant and virally infected cells. The binding of killer cells to their targets is a prerequisite for the lysis of malignant cells by NK cells which utilize cell adhesion molecules (CAMs) to establish initial attachment to target cells. This thesis examined the possibility that defective expression of CAMs on some leukemic cells may be the primary cause of resistance to NK cell-mediated killing. To elucidate the mechanisms by which some leukemic cells an resistant to NK cytotoxicity, a model system was established with the human NK cell line **NK-92**, and the NK resistant leukemic cell line SR-91 which were established and charaterized. SR-91 cells express very low levels of ICAM-1 and they failed to bind to **NK-92** cells. **NK-92** is highly cytotoxic and kills virtually all leukemic cell lines with the only exception being SR-91. Pre-treatment of SR-91 cells with TNF-α or IFN-γ, two cytokines known to upregulate ICAM-1 expression, increased both ICAM-1 expression on SR-91 cells and binding to **NK-92** cells. However, only TNFα treated SR-91 cells became sensitive to killing by **NK-92** cells. The increased binding to **NK-92** cells and sensitivity to their killing were abrogated by anti-LFA-1 antibody or a combination of antibodies against ICAM-1, ICAM-2 and ICAM-3, indicating that LFA-1 interaction with the three ICAMs is essential for effector-target cell binding, which is a prerequisite for subsequent target cell lysis. These results underline the importance of ICAM-1 expression on the target cell SR-91 to allow adequate conjugate formation. However, this is, on its own, insufficient to allow target cell lysis by **NK-92** cells. TNF-α but not IFN-$\gamma,$ also induced the activation of LFA-1, CD44 and $\beta 1$ integrins on SR-91 cells.

Based on these observations, it was hypothesized that the differential effect of TNF-α and IFN-γ could be due to the TNF-α activation of LFA-1 and CD44 on the surface of SR-91 cells that bind to their counter-receptors and activate **NK-92** cells. Preliminary experiments showed that engagement of ICAM-3 and CD44 on **NK-92** cells induced tyrosine phosphorylation of several proteins including the tyrosine kinase $\rm p56\sp{lck}.$ Further confirmation of these results would not only suggest a role for these adhesion molecules in signal transduction events in **NK-92** cells, but perhaps implicates the protein tyrosine kinase $\rm p56\sp{lck}$ as an early intermediate in the subsequent lysis of SR-91 cells. These data suggest that NK resistance of leukemic cells can be overcome by some cytokines. Although increased conjugate formation is induced by both TNF-α and IFN-$\gamma,$ only TNF-α functionally activates LFA-1 and CD44 on target cells that may, upon interaction with counter-receptors on **NK-92** cells induce signal transduction events in the latter that lead to target cell lysis. Therefore, treatment of patients with cytokines to overcome NK cell resistance and to eradicate tumor cells may not only activate and stimulate immune effector cells function but may also have direct effects on leukemic cells to make them more susceptible to the lytic effects of NK cells.